

REPLY

Serial No. 09/954,695
Atty. Docket No. GP116-02.UTRemarks

Claims 1, 7, 8, 10-16, 18, 19, 21, 23, 33-37, 40, 41, 43, 45, 50, 51, 53, 54, 61, 62, 73, 74, 83, 85, 88, 97, 98, 106-108, 110-113, 130-134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153 and 155 are presently pending in the subject application. Claim 21 is withdrawn.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

Claims 17, 38, 52, 71, 92-96, 99-102, 109, 114-124, 135, 137, 139, 141, 143, 145, 147, 149, 152 and 154 are canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a continuing application.

Claims 1, 16, 18, 19, 21, 23, 40, 41, 61, 62, 74, 83, 85, 88, 97, 98, 106, 110-113, 130-134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153 and 155 have been amended herein. No new matter is being introduced in these amendments to the claims.

Claims 1, 19, 21, 23, 41, 62, 74, 83, 85, 88, 110-113 and 151 have been amended to specify that the claimed oligonucleotide or target binding region is at least 18 bases in length and fully hybridizes to the recited target sequence for that oligonucleotide or target binding region. The length limitation of this amendment is supported in the specification at, for example, page 4, lines 22-26 (probes), the sentence bridging pages 5 and 6 (helper oligonucleotides), and page 31, lines 7-9 (amplification oligonucleotides). The "fully hybridizes" limitation of this amendment is supported in the specification *passim* and, for example, in the paragraph bridging pages 17 and 18.

Claims 1, 61, 111, 113, 130, 132 and 134 have been amended to recite a genus-specific probe. With reference to a probe, the term "genus-specific" is defined to mean a probe that is "capable of preferentially hybridizing under stringent hybridization assay conditions to a target nucleic acid sequence present in nucleic acid derived from organisms belonging to at least two species of the genus *Cryptosporidium*." See specification at page 23, lines 3-6.

Claims 16, 18, 40, 97, 98, 106, 130-134, 136, 138, 140, 142, 144, 146, 148, 150, 153 and 155 have been amended to indicate that the base sequence of the oligonucleotide or target binding region of the probe or oligonucleotide is perfectly complementary to the recited target

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sequence. Support for this amendment can be found in the specification at, for example, page 4, lines 22-26, page 5, lines 26-27, page 6, lines 22-23, page 17, lines 21-25, and page 51, lines 1-2.

Applicants wish to express their appreciation for the Examiner's indication that withdrawn claim 21 will be rejoined upon allowance of claim 19.

Objection to the Specification

The disclosure is objected to by the Examiner for containing an embedded hyperlink. The Examiner has requested that Applicants remove the browse executable code. To that end, Applicants have amended the specification herein to render the disclosed hyperlink inactive. Accordingly, withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1, 10, 13-15, 16-19, 23, 38, 40, 41, 43, 45, 50-54, 61, 62, 71, 73, 74, 83, 85, 92-103 (claim 103 was previously canceled by Applicants), 106-124 and 130-155 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Zhu *et al.* (*J. Infectious Disease*, 177:1443-1446 (1998)) in view of Fenger *et al.* (U.S. Patent No. 6,110,665) and Wick *et al.* (U.S. Patent No. 6,063,604) and Williams (U.S. Patent No. 6,146,855) in view of Hogan *et al.* (U.S. Patent No. 5,595,874). Applicants respectfully traverse this rejection for the reasons that follow.

The Examiner relies upon Zhu for teaching a method of detecting *Cryptosporidium* using genus-specific primers from the 18S rRNA. While conceding that Zhu does not teach using SEQ ID NO:1 as the target sequence for the probes and primers, the Examiner points out that Fenger provides a sequence alignment containing the sequences of SEQ ID Nos. 1, 21, 22 and 48 which shows variability between the SRSU sequences of *C. parvum* and non-*Cryptosporidium parvum* organisms in the region of SEQ ID NO:1. Without indicating how Wick is to be read in combination with the other cited references, or what Wick discloses that is not also disclosed by Williams, the Examiner states that Wick provides the entire 18S rRNA gene sequence of *Cryptosporidium parvum*

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and contains the sequences of SEQ ID Nos. 1, 21 and 48. Williams is cited by the Examiner for providing an alignment of the 18S rRNA gene sequences of *C. parvum*, *C. muris* and *C. baileyi* and for showing that the region represented by SEQ ID NO:1 is conserved in these three organisms. Finally, Hogan is cited by the Examiner for teaching a method of comparing rRNA variable region sequences to design probes for distinguishing between organisms. From these disclosures, the Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the genus-specific primers of Zhu using the alignment provided by Fenger and the guidance taught by Hogan to obtain the invention as a whole.

In support of the Examiner's argument that the invention as a whole would have been *prima facie* obvious, the Examiner relies on the Court's holding in *In re Deuel*, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). Specifically, the Examiner quotes a portion of the Court's decision which provides that a *prima facie* case of obviousness is normally based upon structural similarity between a prior art compound and the claimed compound. From this the Examiner argues that the claimed primers simply represent functional equivalents of the probes and primers of Zhu. But whether the claimed compounds perform the same function is not the standard established by the Court in *In re Deuel*, as evidenced by the section quoted by the Examiner, and cannot be relied upon for establishing a *prima facie* case of obviousness. Based on this improper functional equivalence argument, the Examiner goes on to contend that skilled artisans would have been motivated to find alternate compounds with improved properties. However, as Zhu states that primers CF201 and CR201 were specific to the genus *Cryptosporidium* (see Zhu at page 1444, col. 2), the requisite motivation to search for new primers and probes appears to be missing, absent a specific showing by the Examiner.

Applicants further submit that the combination of references relied upon by the Examiner teach away from rather than render obvious the claimed invention. As the Examiner has noted, skilled artisans will generally select regions for probing that have the greatest variability in order to design probes having the greatest specificity for their intended target. See Final Action at

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page 4, lines 20-22, and page 5, line 7 *et seq.* Fenger discloses a region of variability in the 18S rRNA gene sequences of *C. parvum* and other non-*Cryptosporidium* organisms in FIG. 1E that is significantly greater than the region of variability disclosed in FIG. 1A which, if the requisite motivation to identify new probes and primers for detecting *Cryptosporidium* organisms were properly present, might have possibly made it obvious to try designing probes to this region rather than the region targeted by the claimed probes. Moreover, FIG. 3B of Williams discloses that the region of variability disclosed in FIG. 1E in Fenger is conserved among the 18S rRNA gene sequences of *C. parvum*, *C. muris* and *C. baileyi*. Thus, Applicants submit that one skilled in the art at the time of the invention, in possession of the combination of references cited by the Examiner and seeking the greatest degree of probe specificity for detecting *Cryptosporidium* organisms, as argued by the Examiner, would have been led away from the claimed regions.

In addition, Applicants note that the Examiner's rejection of claims 13-15, 41, 43, 45, 83, 85, 100-102, 106-108, 110-113, 115-118, 121-124, 131-134 and 139-146 is improper for failing to address all limitations of these claims. Notwithstanding, Applicants submit that these claims are fully patentable for the reasons stated above for distinguishing the claims over the cited art.

Claims 7, 8, 11-14 and 33-37 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Zhu *et al.* (*J. Infectious Disease*, 177:1443-1446 (1998)) in view of Fenger *et al.* (U.S. Patent No. 6,110,665) and Wick *et al.* (U.S. Patent No. 6,063,604) in view of Hogan *et al.* (U.S. Patent No. 5,595,874) as applied to claims 1-6, 10, 13-15, 16-19, 23, 30, 31, 38-41, 43, 45, 50-54, 61, 62, 71-74, 83, 85 and 92-155 (this combination of references is actually applied to claims 1, 10, 13-15, 16-19, 23, 38, 40, 41, 43, 45, 50-54, 61, 62, 71, 73, 74, 83, 85, 92-102, 106-124 and 130-155 above), and further in view of Becker *et al.* (U.S. Patent No. 6,361,945). Applicants submit that the teachings of Becker do not overcome the deficiencies noted above in the teachings of Zhu and Fenger when combined with the teachings of Wick and Hogan.

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For the reasons set forth above, Applicants submit that the presently pending claims are fully patentable in view of the cited references, considered separately or in any combination. Accordingly, withdrawal of the Examiner's Section 103(a) rejections is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 7, 8, 10-17, 19, 23, 33-38, 40, 41, 43, 45, 50-54, 61, 62, 71, 73, 74, 83, 85, 88, 92-102, 106-118, 130, 131, 135, 137, 139, 140, 143, 145, 149, 151, 152 and 154 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as lacking written description support. Applicants submit that the Examiner's stated basis for this rejection is overcome by the amendments to the claims herein. Specifically, the claims now minimally require that an oligonucleotide or the target binding region of a probe or oligonucleotide be at least 18 bases in length and fully hybridize to the recited target sequence under stringent or amplification conditions. As indicated above in the introductory remarks, an 18 base length minimum for an oligonucleotide or target binding region of a probe or oligonucleotide is supported in the specification at, for example, page 4, lines 22-26 (probes), the sentence bridging pages 5 and 6 (helper oligonucleotides), and page 31, lines 7-9 (amplification oligonucleotides). By "fully hybridizes" is meant that hybridization of the target binding region to the target nucleic acid is limited to the region of the target nucleic acid defined by the recited target sequence. Thus, Applicants submit that the target binding portions of the claimed probes and oligonucleotides are fully described, by sequence, in the specification and, as such, unequivocally evidence that Applicants were in possession of the claimed invention at the time the application was filed. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 7, 8, 10-19, 21, 23, 33-38, 40, 41, 43, 45, 50-54, 61, 62, 71, 73, 74, 83, 85, 88, 92-102, 106-124 and 130-155 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants submit that this rejection is rendered moot by the amendments to the claims. Accordingly, withdrawal of this rejection is respectfully requested.

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Applicants submit that the subject application is in condition for allowance and early Notice to that effect is earnestly solicited.

Please charge any fees due in connection with this Reply, including the fees due for a request for continued examination and a two-month extension of time, to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-872-9306 on the date indicated below to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Respectfully Submitted,



Date: December 6, 2004

By: _____

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